REMARKS

1. Prior Art Issues

1.1. Claims 1-20, 24, 25, 28-36 and 42 stand rejected as obvious over Swierkosz (1989) in view of Tsutsumi (1991), Ouchi et al. (1999), and Osikowicz ('078). This rejection is respectfully traversed.

The present invention discloses a detection kit for rapid detection of RS virus infection by detection of the RS virus particles itself or particles related to RS virus infection. The kit comprises a solid support with an application zone, a detection zone and a positive control zone. Within the application zone moveable conjugates are located. These conjugates are a central part of the invention and contribute to the sensitivity of the kit.

The conjugates of the present invention comprise polymeric carrier molecules whereto one or two (or more) different kinds of targeting species as well as labelling species are linked optionally by connecting moieties. In the application zone the conjugates bind to virus particles or virus related particles produced due to the virus infection, the conjugates move along the solid support and within the detection zone the conjugates with virus particles or virus related particles bind to the solid support. By adjusting (when the detection kits are produced) the amounts of targeting species and labelling species, the conjugate need only to bind to a few virus particles or virus related particles and can, due to a high number of labelling species on the conjugate, develop a signal in the detection zone to indicate the infection. Accordingly, by interposing the polymeric carrier between targeting and labelling species it is possible to design the kit with a variety of sensitivities since the ratio of targeting species to labelling species may be varied.

The conjugate of the present invention may be seen as follows:

targeting species - polymeric carrier - labelling species

wherein the polymeric carrier has a size capable of bearing several targeting species and several labelling species (although claim 1 only requires that each carrier molecule bear one targeting moiety and one labeling moiety).

Swierkosz

Swierkosz et al 1989 describes a procedure wherein specimen in viral transport medium was first treated with sample treatment buffer (reagent 1) and then filtered to clarify the specimen. Microparticles coated with bovine RSV antibody (reagent 2) were added to the specimen simultaneously with biotin-labelled bovine RSV antibody (reagent 3). After a 10-min incubation at room temperature, the solution was transferred to a reaction disk; and alkaline phosphatase-labelled anti-biotin antibody (reagent A), wash (reagent B) and substrate (reagent C) were added sequentially.

As admitted by the examiner, this differs from the claimed invention in that the kit lacks a separate application zone, and in that the positive control zone is not used to confirm movement of the sample, and in that the reference is silent as to how many particles/microliter are detectable.

Swierkosz used microparticles coated with bovine RSV antibody to detect the virus particles of a specimen. These microparticles are different from the conjugate of the present invention as the microparticles were not bound to a labelling species before the virus particles were detected, whereby it is not possible to design a specific predetermined sensitivity.

Tsutsumi

Tsutsumi et al 1999 describes that a swab with virus was placed in 500 ml of Tris-EDTA. The test is a sandwich immuno-assay that uses a paper membrane with a monoclonal antibody in the liquid phase and two polyclonal antibodies in the solid phase. The liquid-phase antibody is a gold colloid-conjugated mouse monoclonal antibody to adenovirus capsid hexon (signal

antibody), while the two solid-phase antibodies are a polyclonal antibody to adenovirus and a polyclonal antibody to mouse immunoglobulin. The signal-antibody segment is adjacent to the round well of the sample aliquot. Briefly, the 10-min one-step procedure is as follows: 200 ml of specimen is transferred to the round well of the testing device. The specimen migrates via capillary action along the membrane, and adenovirus reacts with the signal antibody. Adenovirus-signal antibody complex also reacts with the polyclonal antibody to adenovirus and forms a coloured line that develops within 10 min. The excess signal antibody which does not bind to adenovirus migrates further until it reacts with the polyclonal antibody to mouse immunoglobulin, producing a separate, second coloured line.

In Tsutsumi the moving particle, which is the liquid-phase antibody and also denoted the signal antibody, are gold colloid-conjugated monoclonal antibody to adenovirus capsid hexon. This particle is different from the conjugate comprising a polymeric carrier molecule of the claimed invention, as no polymeric carrier is incorporated in the description of Tsutsumi, whereby it is not possible to design a specific predetermined sensitivity.

Ouchi

Ouchi et al 1999 describes the evaluation of a one step diagnostic test based on an immuno-chromatographic assay which is very easy to perform and results are obtained within 10 min.

Ouchi does not describe any details of the test kit to be used.

Osikowicz

Osikowicz et al (US 5,075,078) discloses a self-performing immunochromatographic device. The testing region includes a patient test bar defined by a first capture reagent specific for the analyte being tested, immobilized on the strip testing region in a generally rectangular configuration. A procedural control

bar defined by a second capture reagent specific for an assay label immobilized on the strip test region in a generally rectangular configuration is also provided in the testing region. The first capture reagent defining the patient test bar comprises immobilized antibody specific for the sample analyte being determined. The second capture reagent defining the procedural control bar comprises immobilized analyte.

The label conjugate used by Osikowicz comprises a monoclonal antibody from a first species specific for the analyte being tested, conjugated to a labelling substance. Preferably the labelling substance is selenium colloid. Moreover, the second capture reagent comprises an antibody from a second species which immunologically reacts with the monoclonal antibody of the first species. The label conjugate does not comprise a polymeric carrier as in the present invention. Osikowicz describes different 'labels' in col. 11 line 33 - col.12 line 20. In col. 12 are mentioned organic polymer latex particles and in col. 12 line 6 reference is made to US patent application Ser. No 248,585, filed Sept. 23, 1988, which is US Pat no. 5,252,459. A copy of US 5,252,459 is enclosed.

Claim 1 of US Pat no. 5,252,459 recites:

> 1. An indicator reagent, useful for determining the presence or amount of an analyte in a test sample, comprising:
>
> a. an **organic polymer latex particle** prepared from the polymerization of a plurality of nonchromophoric monomers, said particle selected from the group consisting of poly(pyrrole), polyphenylene, poly(aniline), poly(thiophene), poly(naphthalene), poly(thiophenol), polyacetylene and derivatives thereof, **said particle having light absorbance characteristics resulting from a conjugated structure from the polymerization of said monomers wherein said polymer latex particle exhibits increased absorbance in the visible spectrum compared to the absorbance in the visible spectrum of the aggregate of nonchromophoric monomers from which it is prepared,** and
> b. a specific binding member directly or indirectly attached to said particle.

The organic polymer latex particles are a labelling particle and do not comprises a polymeric carrier molecule as in the present invention. Thus Osikowicz does not describe a polymeric carrier as in the present invention, instead Osikowicz describes a construct as follows:

targeting species - labelling species

Conclusion

The conjugate described in the present invention is not described in any of the documents referred to by the examiner. The combination of documents as proposed by the examiner will thus not make the present invention obvious.

Furthermore, as mentioned above, the conjugate is an important part of the present invention as the conjugate contributes to the sensitivity of the test kit, where a few virus particles or virus related particles can be caught by the targeting species of the polymeric carrier, and due to many labelling species of each of the polymeric carrier a signal is obtained in the detection zone when the polymeric carrier is caught by first targeting species in the detection zone.

1.2. Claims 21-23, 26, 27, 37-41 and 43 stand rejected over the aforementioned art, further in view of the abstract of Sheeran, et al. (1999). This rejection is respectfully traversed.

Sheeran (1999) describes that the presence of cytokines in children with RSV infection suggests that they have a role in mediating the respiratory tract inflammation induced by RSV.

Sheeran does not give any information about the performance of the test itself and especially not information about the polymeric carrier. For the reasons stated above Sheeran does not contribute to any information making the present invention obvious.

2. Definiteness Issues

2.1. The conjugate in part (iv) of claim 1, 24 and 42 is the same

conjugate as in part (iii), which has been clarified by introducing 'of said' in part (iv).

2.2. The application zone in part (iv) is in liquid contact with the detection zone when the kit is used in an assay. The kit is not necessarily shipped wet as the liquid maybe constituted by a body fluid as can be seen from page 30 line 13 of the description.

2.3. Part (vi) (formerly of claim 1, now recited in new claims 45-47) indicates that the "positive control zone" generates a "positive control confirming the transfer of at least part of said sample from said application zone to said detection zone".

The Examiner questions, "what are the components present in the positive control zone in the claimed kit?"

The "positive control zone" is first referred to at page 28, lines 4-6 of the specification. One implementation of a "positive control zone" is described in Figure 1 and Example 1. As stated at page 49, lines 14-18:

> A control antibody that binds the reporter species independently of the antigen in the urine, was also coupled to the solid surface of the dipstick within the control zone. A red control spot appeared every time in the test regardless whether negative urine or positive urine was used, as an indicator of whether the test was correctly performed. The red colour of this control spot was also produced by accumulation of rhodamine linked to the reporter species.

Plainly, the control antibody is the only required component of the control zone, and its only requirement is that, when immobilized in the control zone, that it bind the reporter species (the conjugate of claim 1, part iii) in some way. Moreover, it would be apparent to a person skilled in the art that the control zone could include, instead of an antibody, any molecule which is capable of binding the reporter species. Cp. the discussion of targeting species at page 34, lines 22-31. Finally, it is not necessary that the control zone element bind the reporter species; a person skilled in the art would realize

that its function could be performed if it bound any part of the mobile phase, i.e., a part of the body fluid sample, or a movable component of the application zone.

2.4. "RS virus related biological cell" has been replaced by "RS virus infected cell", consistent with page 1, lines 5-9 and page 9, lines 4-33 of the specification.

Claims 4-6 have been cancelled.

2.5. Claim 2 refers to the same conjugate as do parts (ii) and (iv) of claim 1. Claim 2 further limits claim 1 by expressly reciting the "connecting moiety". For clarity, the redundant recitation of the polymeric carrier has been excised. In response to the examiner's comment that "nothing can be bound without some sort of connecting moiety" (implying that the connecting moiety of claim 2 was already inherent in the carrier of claim 1), it is noted that claim 2 is directed to those embodiments in which the carrier is derivatized with a reactive group, and is then joined to the other elements of the conjugate by means of that reactive group. In other words, the contemplated "connecting moiety" is one foreign to the carrier, as, in the example, divinylsulfone is to poly dextran.

To clarify, claim 2 now recites that the connecting moiety is foreign to said carrier. We have also excised the roman numeral numbering in claim 2 to avoid confusion with that of claim 1.

2.6. Claims 7 and 29 have been cancelled without prejudice.

2.7. Claim 43 has been amended to recite only the step not already recited in base claim 42, i.e., the detection of the predetermined inflammatory indicator.

2.8. Claim 19 as originally filed recited "according to". In the amendment of August 28, the clean copy left out the "to", but the markup copy retained. We treat claim 19 as if the "to" was retained.

Respectfully submitted,

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